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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/000,297	12/04/2001	Shu Wang	11042-003	8915

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EXAMINER
ROBERTS, PAUL A

ART UNIT	PAPER NUMBER
3731	

DATE MAILED: 07/17/2003

19

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/000,297	WANG ET AL.	
	Examiner	Art Unit	
	Paul A Roberts	3731	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *04 December 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-97* is/are pending in the application.

4a) Of the above claim(s) *1-21,23 and 58-97* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22 and 24-57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *04 December 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *18* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Claim 22 was accidentally grouped into group II because claim 22 was numbered incorrectly by the applicant. Claim 22 should be in group I and the claim is therefore withdrawn from further consideration.

Specification

2. The use of the trademark genePORTER™, Transfast™, etc has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

3. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 38 and 55 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The microporosity of the

outer surface of the wall is not disclosed relative to luminal surface of the conduit. Thus, no critical reason for making the microporosity of the wall surface greater than the luminal surface is disclosed.

5. Regarding claim 55, it is not possible to load 100mm of protein into a 10-micron conduit. The specification only provides enablement for loading 100 microns of protein into a 10-mm conduit.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claim 48 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is not understood what releasing a protein 'progressively' means. The phrase is assumed to mean the protein is released as the microspheres progress in the their dissolution.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

7. Claims 22, 24-27, 47-49 are rejected under 35 U.S.C. 102(e) as being anticipated by Leong et al. US 2002/0155092.

8. The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

9. For the purpose of simplicity, all references that contain multiple inventors (for example Smith et al.) will be referenced by only the first inventor (Smith.) The full name of the inventive identity will be disclosed the first time the reference is cited, and abbreviated in the above manner thereafter.

10. Regarding claims 22, and 24-26, Leong discloses [0649] a tube for regenerating nerve tissue. The tube can contain a poly(phosphoester) polymer (a polymer containing at least 1 phosphoester bond.) In [631] the range of polymer's molecular weight is disclosed to be from 2,000 – 20,000 AMU.

11. Regarding claim 47, the Leong system is designed as a drug delivery system.

12. Regarding claims 48 and 49, the protein delivery system comprises microspheres that contain protein wherein said protein will be inherently released from the microspheres progressively. The microspheres are made from a poly(phosphoester) polymer.

13. Regarding claim 51, the nerve guide can be alternatively made from poly(lactic-co-glycolic acid).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. Claims 27-38 are rejected under 35 U.S.C. 103(a) as being obvious over in Leong '092 in view of Li 5,026,381.

15. The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). For applications filed on or after November 29, 1999, this rejection might also be overcome by showing that the subject matter of the reference and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person. See MPEP § 706.02(l)(1) and § 706.02(l)(2).

16. Regarding claims 27-29, Leong discloses all of claim 22, but doesn't disclose the porosity of the material. However, it is well known in the art to vary the porosity of a material to change the amount of time the material takes to dissolve invitro. At the time of the invention it would have been obvious to one having ordinary skill in the art to make the porosity 8% or 35% to modify the amount of time the material requires for complete dissolution.

17. Regarding claims 30-33, Leong does not disclose the wall thickness of the nerve guide, but nerve guide conduits typically have a wall thickness of about 0.3mm (which includes thicknesses from .21 mm to .39mm). Li 5026381 teaches the thickness of nerve guides, "Typically for a 1mm x .5cm conduit having an overall wall thickness of about .3mm..." At the time of the invention it would have been obvious to one having ordinary skill in the art to make the wall thickness of the Leong device about .3 mm because Li teaches this size is the typical size of a nerve guide.

18. Regarding claims 34-37, the combined Leong device discloses a device with many layers of material (figure 1 of Li shows a multi-layered material). The thickness of the individual layers is not disclosed. It would have been an obvious matter of design choice to modify the Leong-Li device to have a wall layer thickness of 25 micrometers since the applicant has not disclosed the layer thickness of 25 micrometers would solve any stated problem or is for any particular purpose and it appears that the undisclosed layer thickness of Li would perform equally well.

19. Regarding claim 38, the combined Leong device does not disclose that the outer surface of the wall has greater microporosity than the luminal surface of the conduit. It would have been an obvious matter of design choice to modify the Leong-Li device to have a wall layer thickness

of 25 micrometers since the applicant has not disclosed the layer thickness of 25 micrometers would solve any stated problem or is for any particular purpose and it appears that undisclosed microporosity relationship between the said surface of the Leong device would perform equally well.

20. Claims 39, 40, 42-44, 46, 50, 56, and 57 are rejected under 35 U.S.C. 103(a) as being obvious over in Leong '092 in view of Peulve et al. 2002/0071828, in further view of Neuman et al 2003/0027779, Mao et al. 6485737, and Stone 5258043. Note, the applied references have an inventor in common with the applicant. See above.

21. Regarding claim 39, though the Leong reference discloses a nerve guide, it does not suggest using a gene delivery system. Such systems are taught by Peulve in [0079] are used to improve nerve tissue regrowth. At the time of the invention it would have been obvious to one having ordinary skill in the art to add the Peulve gene delivery system to the Leong device to help stimulate nerve tissue regrowth.

22. Regarding claim 40, the Peulve-Leong device discloses ('828 [0041]) the use of a complex of DNA and a cationic polymer or lipid loaded into a cuff.

23. Regarding claims 41, 52, and 53, the Peulve-Leong device discloses the size of the complex's particles to be 5 microns and at the time of the invention it would have been obvious to one having ordinary skill in the art to vary the size of the particles to change the rate of the dissolution of the microparticles to 10 microns to enable the conduit to be useful for delivery different proteins that would require slower dissolution.

24. Regarding claim 42, the Peulve-Leong device discloses the incorporation of polyethylenimine into the cationic polymer [0041].

25. Regarding claim 43, the Peulve-Leong device doesn't disclose the incorporation of phosphatidylethanolamine, but this compound is a well known gene delivery agent. Neuman et al '779 discloses the method of injecting DNA directly into a nerve cell using said compound as the delivery agent. At the time of the invention it would have been obvious to one having ordinary skill in the art to use phosphatidylethanolamine as the drug delivery agent for the Puelve-Leong conduit because Neuman teaches this agent can be used to transmit DNA into nerve cells.

26. Regarding claim 44, the Peulve-Leong device doesn't disclose the incorporation of GenPORTER™, but this compound is a well-known gene delivery agent. GenePORTER™ is a commercial product designed to transfer DNA to a cell. At the time of the invention it would have been obvious to one having ordinary skill in the art to use a commercial gene delivery product to delivery genetic information.

27. Regarding claim 45, the Peulve-Leong device doesn't specifically disclose that the gene encodes a neurotrophic protein, but this step is inherent because DNA's intrinsic function in nerve cells is to encode neurotrophic proteins.

28. Regarding claims 46 and 56, the Peulve-Leong device discloses that BDNF ('828 [024]) is a preferred neutrophin to use in the gene delivery system of Peulve.

29. Regarding claim 50, the Peulve-Leong device doesn't disclose which subunit the conduit contains, but the claimed subunit is obvious to use because it is biodegradable (bioabsorbable). Mao teaches the use of the claimed subunit and incorporates its use in a bioabsorbable polymeric implant. Col 1, lines 20-30 explain using the claimed subunit is beneficial because bioabsorbable compounds obviate the need to invasively remove the device. At the time of the

invention it would have been obvious to one having ordinary skill in the art to use the Mao subunit in the Leong conduit to provide the Leong conduit with bioabsorbable qualities.

30. Regarding claim 55, the Peulve-Leong device doesn't disclose the length of protein to be loaded per length of conduit. It would have been an obvious matter of design choice to modify the Peulve-Leong device to have the 10 microns of protein to be loaded per 10 mm of conduit since the applicant has not disclosed this loading procedure would solve any stated problem or is for any particular purpose and it appears that the undisclosed amount of protein added by Peulve would perform equally well.

31. Regarding claim 57, the Peulve-Leong device doesn't disclose the conduit should contain Schwann cells, but adding Schwann cells to a nerve guide is a well-known beneficial procedure. Stone 5258043 teaches this procedure and explains it aids in nerve tissue regrowth. At the time of the invention it would have been obvious to one having ordinary skill in the art to seed the nerve guide of Leong device with Schwann cells, because Stone teaches doing so will result in greater nerve regrowth.

32. Claim 54 is rejected under 35 U.S.C. 103(a) as being obvious over in Leong '092. Leong discloses the nerve conduit should release protein from the microspheres, but does not disclose for what temporal duration the microspheres should release the protein. Providing the nerve cells with a long, constant source of protein will improve the regenerative qualities of the procedure. At the time of the invention it would have been obvious to one having ordinary skill in the art to modify the Leong device so that microspheres will dissolve very slowly thus releasing the protein for three months or longer, and thereby improving the regenerative qualities

of the procedure. Also, methods of modifying the microspheres' longevity are well known in the art. Increasing porosity or surface area of the sphere will result in faster dissolution times.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

US 20020012660 A1 Colman, Alan et al. method of preparing a somatic cells for nuclear transfer

US 20020137814 A1 Dang, Wenbin et al. Biodegradable compositions comprising poly(cycloaliphatic phosphoester) compounds, articles, and methods for using the same

US 20020172717 A1 Leong, Kam W. et al. Systemic delivery of compounds through non-invasive bladder administration

US 20030028204 A1 Li, Shu-Tung et al. Implant devices for nerve repair

US 4886870 A D'Amore, Patricia et al. Bioerodible articles useful as implants and prostheses having predictable degradation rates

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Paul A Roberts whose telephone number is (703) 305-7558. The examiner can normally be reached on 7:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Milano can be reached on 703-308-2496. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3590 for regular communications and (703) 305-3590 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0858.

Paul Roberts
July 8, 2003

MICHAEL J. MILANO
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